IN THE SPECIFICATION*:

Pg. 1, below the title, add the following paragraphs:

This application is a divisional of co-pending application number 09/829,855, filed April 10, 2001, which in turn claims the benefit of United States provisional application number 60/196,063, filed April 10, 2000 and United States provisional application number 60/196,258, filed April 11, 2000.

This Invention was made with Government support under Contract No. DE-FC36-01GO11016 awarded by the Department of Energy. The Government has certain rights in this invention.

Replace the paragraph on pg. 12, lines 19-20 with the following:

Figure 12 shows oligonucleotides useful for amplifying nucleic acid molecules for SARD.

Replace the paragraph on pg. 12, lines 21-24 with the following:

Figure 13 shows the use of the SARD strategy for Eubacteria. The double-underlined sequence and the wavy-underlined sequence represent the sequence tags for the two pools and the single-underlined sequence delineates the *Bpm*I recognition site.

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* An "Appendix to Specification Amendments" is enclosed at Tab A, showing the amendments to the specification. In that Appendix, the added portion of text is underscored and the deleted portion is bracketed.

Replace the paragraph on pg. 12, lines 25-26 with the following:

Figure 14 is a graphical representation of a SARD analysis of a defined population.

Replace the paragraph on pg. 12, line 27 to pg. 13, line 1 with the following:

Figure 15 shows the sequence of SARD tags identified from Wy-1 sample. The number in parentheses indicates the number of tags having that sequence.

Replace the paragraph on pg. 13, lines 2-3 with the following:

Figure 16 shows SARD tags identified from Wy-2 sample. The number in parentheses indicates the number of tags having that sequence.

Replace the paragraph on pg. 13, lines 4-6 with the following:

Figure 17 is a graphical representation of the number and abundance of SARD tags. The upper panel shows the Wy-1 SARD Tag Diversity Profile and the lower panel shows the Wy-2 SARD Tag Diversity Profile.

Replace the paragraph on pg. 17, lines 7-25 with the following:

Step I. Sample Preparation and DNA Amplification by PCR

Samples may be obtained from any organism or region desired. For environmental microbial analyses, samples may be obtained from, without limitation, buildings, roadways, soil, rock, plants, animals, cell or tissue culture, organic debris, air or water. For medical microbial analyses, samples may be obtained from, without limitation, humans, animals, parasites, water, soil, air and foodstuffs. For viral analyses, samples may be obtained from, without limitation, viral culture stocks, humans, animals, plants, cell or tissue culture and microbes. For immunoglobulin or TCR analyses, samples may be obtained from, without limitation, humans, animals or cell or tissue cultures. DNA molecules from the sample of interest may be isolated by any method known in the art. See, e.g., Sambrook et al., 1989 and Ausubel et al., 1992. In a preferred embodiment, DNA is obtained as described by Yeates et al., "Methods for Microbiological DNA Extraction from Soil for PCR Amplification," Biological Procedures Online, Volume 1, May 14, 1998, available through the Internet; Liu et al., Applied and Environmental Microbiology (1997) 63: 4516-4522; and Tsai et al., Applied and Environmental Microbiology (1992) 58: 2292-2295. The DNA molecules do not have to be completely purified but only need be isolated to the point at which PCR may be performed.

Replace the paragraph on pg. 24, lines 8-17 with the following:

The invention is directed toward methods of analyzing the genetic diversity of a population in a sample. Each population that is analyzed will have its own unique set of different organisms or genes. The data set that is captured from each sample

should recapitulate the genetic structure in a survey format to include a marker for each gene or organism and the relative abundance of each gene or organism in the population as a whole. The markers for a particular population form a marker diversity profiles (MDPs), that may be entered into a database. See, e.g., Figure 8 which shows one schematic for generating such a database. The method by which the data are captured is not critical as long as it produces an accurate representation of each population.

Replace the paragraph on pg. 25, lines 3-13 with the following:

A marker may be correlated with a particular condition or with another marker. See, e.g., Figure 9 for a schematic of the steps involved in determining particular parameters associated with an MDP and Figure 10, which shows a schematic for generating a marker diversity matrix database. A condition or state may be an environmental condition such as pH, temperature, salinity, or the presence or absence of an organic or inorganic compound such as hydrocarbons, nitrates or mineral deposits. A condition may be a physiological or medical condition such as an acute or chronic disease state, physiological state, developmental stage or associated with a particular body tissue or fluid. Information regarding all known parameters associated with the samples will also be saved together with the MDPs.

Replace the paragraph on pg. 25, lines 14-22 with the following:

Each MDP is composed of markers which represent a small number, more preferably one, species or gene. For instance, in the case of Example 1, each marker would be comprised of a 12 base-pair polymorphic 16S rDNA sequence. Such parameters that relate to environmental samples may include inorganic components (obtained through atomic adsorption analysis), organic components (obtained through GC-MS or LC-MS), grain size analysis, pH, and salinity. Parameters that relate to medical samples would include, but are not limited to, a complete medical history of the donor. See, e.g., Figure 11, which shows a schematic for mapping applications using marker diversity profiles.

Replace the paragraphs on pg. 45, lines 7-25 with the following:

In the Wy-1 sample, 58 distinct tags were identified and the abundance of each tag varied. The most abundant tag (ATGGCTGTCGTCAGCT) (*SEQ ID NO: 6*) made up about 34% of the population. This tag sequence is identical to many bacterial sequences in GenBank and its position within the 16S rDNA gene indicates that it is located in a conserved region located distal to the targeted *AluI* restriction site. In other words, the contributing 16S gene(s) for this tag did not contain the conserved *AluI* site. Since the SARD tag position is dictated by the first *AluI* site distal to the biotinylated primer used in the initial PCR reaction, it is likely that the first *AluI* site in the contributing 16S gene(s) was located downstream within a conserved region. In order to decrease the number of tags that do not contain the conserved *AluI* site next to the polymorphic region, one may gel

purify the approximately 100 basepair PCR products after the first *Alu*I restriction step. However, this may result in losing some information. Nevertheless, 39% of the tags (58/148) in this set were different from each other. See Figures 15 and 17.

The Wy-2 sample was found to contain 79 different tags out of a total of 234 tags that were examined. Thus, 34% of the tags (79/234) in this set were different from each other. See Figures 16 and 17. As in the case with Wy-1, the tag ATGGCTGTCGTCAGCT (SEQ ID NO: 6), which represents a conserved sequence in a 16S rDNA gene, was most abundant and made up about 30% of the population.

Replace the paragraph on pg. 46, lines 16-21 with the following:

In this example, the following oligonucleotides are designed: 5' biotin-TA(CT)T(CT)CCCA(GA)GCGG(CT)(GCT)(GC)(GA)CTT(AGCT)-3' (SEQ ID NO: 155) corresponding to position 817-838 of the *Methanococcus jannaschii* 16S rDNA gene (GenBank Accession number M59126), and (5'-GGTG(TGC)CA(GC)C(CA) GCCGCGGTAA(TC)ACC(AGCT)-3' (SEQ ID NO: 156) corresponding to position 457-481 of the *Methanococcus jannaschii* 16S rDNA gene.

Replace the paragraph on pg. 49, lines 13-19 with the following:

An example of such a collection of degenerate oligonucleotides for the domain Bacteria could include permutations

of the following primer: 5'- AACGAGCGCAACCNNNNNNNNN-3' (SEQ ID NO: 157), where N indicates any nucleotide at that position. This sequence corresponds to position 1101-1122 of the *E. coli* 16S rDNA gene (GenBank Accession number E05133). Alternatively, the primers could be designed such that they are composed of a mixture of constant sequence, semi-degenerate positions (e.g. A or G) and degenerate positions (e.g. A, G, C or T).

Replace the Tables I-III on pages 50-54 with the following:

Table I*

Species	GenBank Acc#	Tag Sequence	Position	SEQ ID NO:
Desulfurobacterium thermolithotrophumA	J001049	GTCAGTTGCCGAAGCT	814-829	158
Uncultured Aquificales OPS132	AF027104	GTCCGTGCCGTAAGCT	810-825	159
Bacteroides caccae	X83951	ATGGTTGTCGTCAGCT	1021-1036	160
Actinomyces bovis	X81061	TTTCCGCGCCGTAGCT	834-849	161
Actinomyces meyeri	X82451	TTTCTGCGCCGTAGCT	828-843	162
Denitrobacterium detoxificans	AF079507	CCTCCGCGCCGCAGCT	788-803	163
Uncultured GNS bacteria BPC110	AF154084	CCCGGTAGTCCTAGCT	765-780	164
Uncultured GNS bacteria GCA004	AF154104	CATCGGTGCCGCAGCT	824-839	165
Uncultured GNS bacteria GCA112	AF154100	CGGCGGTGCCGTAGCT	826-841	166
Acetobacter aceti	AF127399	ACTCAGTGTCGTAGCT	782-797	167
Gluconobacter asaii	AB024492	ACTCAGTGTCGAAGCT	783-798	168
Burkholderia sp. JB1	X92188	CCTTAGTAACGAAGCT	837-852	169
Denitrobacter permanens	Y12639	ACGATGTCAACTAGCT	789-804	170
Desulfobacter curvatus	M34413	CTGCTGTGCCNAAGCT	861-876	171
Desulfobulbus sp. BG25	U85473	CCTCTGTGTCGCAGCT	854-869	172
Legionella anisa	X73394	ACGATGTCAACTAGCT	790-805	173
Benzene mineralizing clone SB-1	AF029039	ATGGTTGTCGTCAGCT	1029-1044	174
Escherichia coli	E05133	CGTGGCTTCCGGAGCT	848-863	175
Uncultured Acidobacterium Sub.Div-1	X68464	CCGCCGTGCCGAAGCT	813-828	176
Uncultured Acidobacterium Sub.Div-1	Z73363	CGGCTGTGCCGAAGCT	521-536	177
Uncultured Acidobacterium Sub.Div-1	Z73365	CCACTGTGCCGTAGCT	521-536	178
Uncultured Acidobacterium Sub.Div-1	Z73368	CTGCTGTGCCGCAGCT	521-536	179
Uncultured Acidobacterium Sub.Div-1	Z73364	CTGCCGTGCCGGAGCT	521-536	180
Uncultured Acidobacterium Sub.Div-1	U68659	CCAATGTGCCGGAGCT	319-334	181
Uncultured Acidobacterium Sub.Div-1	D26171	CCGTCGTGCCGTAGCT	79-794	182
Uncultured Acidobacterium Sub.Div-1	X97101	CCGTCGTGTCGTAGCT	687-702	183
Uncultured Acidobacterium Sub.Div-1	X97098	CTGCCGTGTCGAAGCT	798-813	184
Uncultured Acidobacterium Sub.Div-1	AF047646	CTCCCGTGTCGAAGCT	779-794	185

Uncultured Acidobacterium Sub.Div-1	AF050548	CCGCCGTGCCGGAGCT	316-331	186
Uncultured Acidobacterium Sub.Div-2	U68612	CTGAGGAACGAAAGCT	226-241	187
Uncultured Acidobacterium Sub.Div-2	Y07646	GTGTCGTCCCGGAGCT	830-845	188
Uncultured Acidobacterium Sub.Div-3	X97097	GGGCTGTGCCGAAGCT	804-819	189
Uncultured Acidobacterium Sub.Div-3	X68466	GGTCGGTGCCGGAGCT	796-811	190
Uncultured Acidobacterium Sub.Div-3	X68468	GGTCGGTGCCAGAGCT	796-811	191
Uncultured Acidobacterium Sub.Div-3	U68648	GGTTCGTGCCGGAGCT	317-332	192
Uncultured Acidobacterium Sub.Div-3	X68467	TGTCTGTGCCGGAGCT	796-811	193
Uncultured Acidobacterium Sub.Div-3	AF013515	TATCCGTGCCGGAGCT	799-814	194
Uncultured Acidobacterium Sub.Div-3	AF027004	GGTCCGTGCCGGAGCT	778-793	195

* Sequences shown in bold with shadow indicates they are not unique to this set.

Table II

Species	GenBank Acc#	Tag Sequence	Position	SEQ ID NO:
Crenarchaeota				
Aeropyrum pernix	D83259	CTAGGGGGCGGGAG	614-627	196
Desulfurococcus mobilis	M36474	CTAGGTGTTGGGTG	856-869	197
Staphylothermus marinus	X99560	CTAGGTGTTGGGCG	770-783	198
Metallosphaera sedula	X90481	CTAGGTGTCGCGTA	756-769	199
Sulfolobus acidocaldarius	D14053	CTAGGTGTCGAGTA	785-798	200
Sulfolobus metallicus	D85519	CTAGGTGTCACGTG	744-757	201
Caldivirga maquilingensis	AB013926	CTAGCTGTTGGGTG	773-786	202
Pyrobaculum islandicum	L07511	CTAGCTGTCGGCCG	781-794	203
Euryarchaeota				
Archaeoglobus fulgidus	X05567	CTAGGTGTCACCGA	780-793	204
Archaeoglobus veneficus	Y10011	CTAGGTGTCACCGG	758-771	205
Haloarcula japonica	D28872	CTAGGTGTGGCGTA	762-775	206
Halococcus morrhuae	D11106	CTAGGTGTGGCGTT	765-778	207
Methanococcus jannaschii	M59126	CTAGGTGTCGCGTC	768-781	208
Methanobacterium bryantii	AF028688	None		
Methanobacterium subterraneum	X99045	None		
Pyrococcus abyssi	Z70246	CTAGGTGTCGGGCG	767-780	209
Picrophilus oshimae	X84901	CTAGCTGTAAACTC	742-755	210

Table III

Species	GenBank Acc#	Peptide Sequence	M.W.	Position	SEQ ID NO:
Desulfurobacterium thermolithotrophum	AJ001049	RAQPLSLVASG*	1097.40	1079-1136	211
Uncultured Aquificales OPS132	AF027104	RAQPLSCVTSG*	1117.40	1074-1131	212
Bacteroides caccae	X83951	RAQPLSSVTNRSC*	1417.70	1069-1126	213
Actinomyces bovis	X81061	RAQPLSRVASTLWWGLAGD	2083.60	1088-1145	214
Actinomyces meyeri	X82451	RAQPLPYVASTLWWGLVGD	2128.60	1082-1139	215
Denitrobacterium detoxificans	AF079507	RAQPLPHVASIRLGTHGG	1866.50	1039-1094	216
Uncultured GNS bacteria BPC110	AF154084	RAQPLLYVIRVIPD	1652.10	1074-1116	217
Uncultured GNS bacteria GCA004	AF154104	RAQPSLYVTRIIRD	1687.10	1080-1122	218
Uncultured GNS bacteria GCA112	AF154100	RAQPSPYVIRVIRD	1669.00	1082-1124	219
Acetobacter aceti	AF127399	RAQPLSLVASMFGWAL*	1746.30	1038-1095	220
Gluconobacter asaii	AB024492	RAQPLSLVASTFRWAL*	1815.30	1034-1092	221
Burkholderia sp. JB1	X92188	RAQPLSLVATQEHSRET	1922.20	1094-1144	222
Denitrobacter permanens	Y12639	RAQPLPLVATFSWAL*	1669.10	1077-1131	223
Desulfobacter curvatus	M34413	RAQPLSLVASTLCGNSNET	1960.40	1116-1172	224
Desulfobulbus sp. BG25	U85473	RAQPLPLVASSSAGHSKGT	1863.40	1114-1170	225
Legionella anisa	X73394	RAQPLSLVAST*	1141.40	1078-1135	226
Benzene mineralizing clone SB-1	AF029039	RAQPLPLVANRSSWGL*	1764.20	1077-1134	227
Escherichia coli	E05133	RAQPLSFVASGPAGNSKET	1916.30	1103-1159	228
Uncultured Acidobacterium Sub.Div-1	Z73363	RAQPLSLVASGSSRAL*	1612.10	775-832	229
Uncultured Acidobacterium Sub.Div-1	Z73365	RAQPLSSVAIGSSRATLAK	1912.50	777-835	230
Uncultured Acidobacterium Sub.Div-1	Z73368	RAQPLFASCHH*	1933.50	779-835	231
Uncultured Acidobacterium Sub.Div-1	Z73364	RAQPLFAQLPSFSWALCRN	2204.80	778-835	232
Uncultured Acidobacterium Sub.Div-1	U68659	RAQPLLPXAII*	1218.70	573-630	233
Uncultured Acidobacterium Sub.Div-1	D26171	RAQPLLPVATI*	1177.50	1035-1090	234
Uncultured Acidobacterium Sub.Div-1	X97101	RAQPLSPVAII*	1163.50	943-998	235
Uncultured Acidobacterium Sub.Div-1	X97098	RAQPLSSVATI*	1141.40	1054-1109	236

Uncultured Acidobacterium Sub.Div-1	AF047646	RAQPLFLVATI*	1227.60	1035-1090	237
Uncultured Acidobacterium Sub.Div-1	AF050548	RAQPSSLVANTLW*	1441.70	572-629	238
Uncultured Acidobacterium Sub.Div-2	U68612	RAQPLHVVATRKRELYVD	2150.60	577-630	239
Uncultured Acidobacterium Sub.Div-2	Y07646	RAQPLHVVATPQGGTLRG	1857.30	1085-1140	240
Uncultured Acidobacterium Sub.Div-3	X97097	RAQPSSLVANPQGKHPKGT	1972.40	1060-1116	241
Uncultured Acidobacterium Sub.Div-3	U68648	RARPLSCVAII*	1197.70	574-629	242
Uncultured Acidobacterium Sub.Div-3	AF013515	RAQPLSCVANPQGCTLRR	1969.50	1057-1112	243
Uncultured Acidobacterium Sub.Div-3	AF027004	RAQPSPCVATPPRAGALSGD	1950.40	1036-1096	244

* Indicates an in-frame stop codon was encountered within the polymorphic sequence.